Discussion

The results of this study in man, although its scale was limited, are consistent with experiments in animals. Normal rats treated with isoniazid showed no significant gain in weight (Benson *et al.*, 1952; Rubin *et al.*, 1952), and in dogs there was no change in metabolic rate (Rubin and Burke, 1953). In man, Faloon (1953) found no change in nitrogen balance, appetite, or food intake in three patients with non-tuberculous disease given isoniazid for six to eight days. The observations here presented provide no evidence that isoniazid has any effect in causing gain in weight in the normal human male. In view of the negative results, we do not contemplate engaging in a trial on a larger scale. It seems doubtful whether the minor side-effects noted above were attributable to isoniazid.

Summary

The average weekly weight gain in four healthy males receiving isoniazid for eight weeks was similar to the gain in the same group treated for two weeks with control capsules containing lactose and to the gain during four weeks on observation alone. The average weekly gain was less than that of a similar group of four males treated for 10 weeks with control capsules containing lactose. We have therefore obtained no evidence to suggest that isoniazid in tuberculous patients has an effect on weight gain other than that due to its effect on the disease. No side-effects were recorded which could be attributed with certainty to isoniazid. One member of the treated group became unduly sleepy; another experienced Raynaud's phenomenon for the first time. One of the control group experienced an unexpected increase in cheerfulness, but no change in emotional tone was recorded by any member of the treated group.

We are most grateful to our colleagues who cheerfully put up with the inconveniences of the trial. We also record our gratitude to Messrs. E. R. Squibb and Sons for a generous gift of the isoniazid and control capsules. This investigation is one of a series supported by a grant from the Royal Victoria Hospital Tuberculosis Trust.

REFERENCES

- Benson, W. M., Stefko, P. L., and Roe, M. D. (1952). *Amer. Rev. Tuberc.*, **65**, 376.
 Faloon, W. W. (1953). *Ibid.*, **68**, 207.
 Medical Research Council (1952). *British Medical Journal*, **2**, 735.
 — (1953). *Ibid.*, **1**, 521.
 Rubin, B., and Burke, J. C. (1953). *Amer. Rev. Tuberc.*, **67**, 644.
 — Hassert, G. L., jun., Thomas, B. G. H., and Burke, J. C. (1952). *Ibid.*, **65**, 392.

The annual report of the Fountain Hospital, the 600-bedded hospital at Tooting Grove for mentally defective children from London and Surrey, draws attention to Section 3 of the Mental Deficiency Act, which allows a child to be placed in hospital by the parents without the need of a magistrate's order. Of the 84 certified direct admissions to the Fountain Hospital during 1953, over 80% were admitted under this procedure. The admission of young children without any legal formalities, the report continues, would go a long way towards improving the public's attitude to mental deficiency in young children. Indeed, a plea is made that this should be tried out experimentally. "If the Fountain Hospital, owing to its special circumstances, could be exempted for a temporary period from the normal working of the Mental Deficiency Acts experience would be gained in the *voluntary* care of defective children, comparable to that made possible by the Mental Treatment Act of 1930. This evidence might be of considerable value to the Royal Commission inquiring into the certification and detention of mental patients."

BLOOD GROUPS AND GYNAECOLOGICAL CANCER

BY

ERIK KROKFORS, Med.lic.

AND

OLAVI KINNUNEN

Lecturer in Gynaecology, Assistant Physician-in-Chief
(From the Women's Clinic I and II, Helsinki, Finland)

Stocks showed in 1950 that the standardized mortality of cancer of the stomach tended to be greater in northern than in southern towns in England. He assumed this to be connected with the fact that gastric cancer depends on an irritant. In an attempt to explain the variations in mortality, Aird, Bentall, and Roberts (1953) demonstrated that the frequency of blood group A was greater in patients suffering from gastric cancer than in the general population of the same locality. They collected their series from a number of hospitals in England and Scotland, using as controls an equal number of patients chosen at random from the same hospital or, where this was difficult, estimating an equal control number from the blood-group frequencies in large numbers of the local population. In most cases diagnosis was confirmed by a histological report; in only a few cases were the authors dependent on radiological findings or on the clinical picture alone.

Table I shows the results of Aird, Bentall, and Roberts. It indicates that in different parts of England and Scotland the frequency of blood group A was

TABLE I

	Cancer Cases				Controls			
	O	A	B	AB	O	A	B	AB
Newcastle (101 cases)	43.6	43.6	11.9	1.0	52.5	37.4	7.6	2.5
Leeds (217 cases)	42.4	47.9	7.4	2.3	46.5	40.3	7.1	6.2
Manchester (771 cases)	44.7	44.5	6.4	3.8	52.1	38.4	7.0	2.5
Liverpool (217 cases)	39.2	44.7	12.4	3.7	49.7	39.6	7.8	2.7
Birmingham (100 cases)	37.0	57.0	3.0	3.0	49.6	44.4	3.0	3.0
Total of Northern England (1,406 cases)	42.9	46.4	7.6	3.1	50.7	39.3	6.8	3.2
London (1,340 cases)	43.1	46.0	7.9	2.9	45.8	42.2	8.9	3.1
Scotland (478 cases)	51.2	36.4	9.6	2.7	52.6	32.5	11.7	3.1
Overall figures (3,632 cases)	44.5	44.8	7.8	2.9	48.6	39.8	8.3	3.2

greater and that of blood group O correspondingly less in patients with cancer of the stomach than in the general population.

Our Own Investigations

It seemed of interest to make a corresponding study of the distribution of the blood groups in patients suffering from gynaecological cancer. Our series consists of 300 patients with uterine or other gynaecological cancer whose blood groups had been determined; they were treated at the Women's Clinic of the University of Helsinki during the period 1948-53. Diagnosis was confirmed in all cases by a histological report. Owing to the centralization of hospital conditions in Finland, the majority of all cases of gynaecological carcinoma, both operative cases and those given radiation, are treated at the Women's Clinic in Helsinki. This being so, the patients no doubt represent a cross-section of the population as regards distribution of blood groups. The control series was therefore selected on a similar basis.

All such acute cases of gynaecological disease as are predominantly from Helsinki or its immediate vicinity—for example, abortions and extrauterine pregnancies—were excluded. We also used for control purposes the data published by Streng and Ryti (1927) regarding blood-group distribution in the general population of Finland.

Table II compares our results with the data obtained by Streng and Ryti.

TABLE II

	Gynaecological Cancer				Controls			
	O	A	B	AB	O	A	B	AB
Krokfors and Kinnunen	113 37.7%	110 36.7%	57 19%	20 6.7%	98 31.6%	139 44.8%	48 15.5%	25 8.1%
Streng and Ryti					33.5%	42.7%	16.8%	7.0%

Comparison of the control data in Tables I and II shows, first, that the frequency of blood group O is considerably less and that of groups B and AB correspondingly greater in the general population of Finland than in that of England and Scotland. Group A is about equally frequent in both countries. But when we compare the distribution of blood groups in our carcinoma patients and in our controls we find that blood group O seems to predominate clearly in the cancer group, blood group A having a correspondingly lower frequency.

We subclassified our cancer group into cancer of the uterus and other gynaecological cancer, and this seemed to cause no appreciable changes in the distribution of the blood groups (Table III).

TABLE III

	O	A	B	AB
Cancer of the uterus	37.9%	37.1%	18.5%	6.5%
Other gynaecological cancer	36.5%	36.5%	20.0%	7.0%

It occurred to us that there might be a correlation between the blood group and the age of the patient at the onset of gynaecological cancer. We therefore studied separately 100 patients, the youngest in the series. Their upper age limit was 45 years. The blood groups were as follows: O, 42%; A, 33%; B, 17%; and AB, 8%. The relatively greater frequency of blood group O thus seemed to increase further when this subdivision was made.

Conclusion

On the basis of our own studies we can only state briefly that, in contrast to the English series of cancer of the stomach, a Finnish series of gynaecological cancer showed a clearly lower frequency of blood group A than the corresponding controls. It seemed, on the contrary, that the incidence of blood group O was particularly high in our series of gynaecological cancer; this appeared most distinctly in the youngest patients studied.

REFERENCES

- Aird, I., Bentall, H. H., and Roberts, J. A. F. (1953). *British Medical Journal*, 1, 799.
 Stocks, P. (1950). *Brit. J. Cancer*, 4, 147.
 Streng, Osw., and Ryti, Elsa (1927). *Acta Soc. Med. "Duodecim"*, 8, 1.

From May 16 margarine must contain between 760 and 940 international units of vitamin A per ounce and between 80 and 100 international units of vitamin D per ounce. This vitamin-A content is roughly equivalent to that of butter. This Order applies to all home-produced and imported margarine sold by retail, including margarine sold as such by a caterer but not margarine used by him in made-up foods or in cooking. It does not apply to sales of margarine to a caterer.

Medical Memoranda

Extreme Sensitivity to Insulin

Since its introduction by Sakel in 1935, treatment by insulin has been widely used in various forms of mental illness. Considerable variations have been experienced in the reaction of patients to insulin, and it is generally agreed that there is marked individual sensitivity to the drug (Tennent, 1944). Success in the induction of coma has been reported with doses of 15 units (James *et al.*, 1938) and of 18 units (Parfitt, 1937). A case is described in which coma was induced with a dose of 2 units, and a method of desensitization is given. I have been unable to trace any record in the literature of coma being induced with such a small amount of insulin.

CASE REPORT

An unmarried woman aged 19 suffering from anorexia nervosa was referred to Fulbourn Hospital, Cambridge, for a course of modified insulin on July 20, 1953. Her weight at this time was 5 st. 7½ lb. (35 kg.).

The initial dose (see Table I) was 15 units, given intramuscularly at 7.15 a.m. At 9.30 a.m. she was in sopor and showed loss of a normal response to speech and

TABLE I

Days	Units of Insulin Given at 7.15 a.m.	Time of Sopor	Time of Coma
1	15	9.30 a.m.	10.5 a.m.
2	10	9.50 "	10.0 "
3	1	No reaction	No reaction
4	3	10.15 a.m.	10.25 a.m.
5	Sterile water	No reaction	No reaction
6	2	10.0 a.m.	10.30 a.m.

impairment of orientation. At 10.5 a.m. she was in coma; she showed loss of all purposive responses, none being elicited from visual, auditory, or tactile stimuli. The next day the dose was reduced to 10 units, and sopor was produced at 9.50 a.m. and coma at 10 a.m. Because of this marked sensitivity, the following morning she received only 1 unit. This produced no effect. The next day the amount of insulin was raised to 3 units, and sopor came on at 10.15 a.m. and coma at 10.25 a.m.

To ensure that it was in fact the insulin which was causing these reactions, on the succeeding morning an intramuscular injection of sterile water was given at 7.15 a.m., but this had no effect whatever on the patient. At the same time a specimen of blood was taken in order to ascertain the fasting blood sugar. This was 0.72 g. per 100 ml. The next morning 2 units of insulin was given, and this time sopor was induced at 10 a.m. and coma at 10.30 a.m.

It was decided to attempt to desensitize the patient by starting at a dose of 0.2 unit and increasing this by 0.2 unit daily. This proved successful, and by December 18 she was having 17 units daily, which was enough to induce drowsiness but not to produce sopor or coma. Her weight was then 6 st. 2 lb. (39 kg.).

COMMENT

It is known that insulin hypersensitivity is present in clinical cases of hypopituitarism—for example, Simmonds's disease (Wright, 1952). As the physical picture of this disease may closely resemble the classical "anorexia nervosa" and as there may be a secondary disturbance of pituitary function in the later and more severe stages of anorexia nervosa, the patient was investigated to discover if any pituitary dysfunction was present. The following factors were in favour of anorexia nervosa: she was a young unmarried woman of a neurotic obsessional personality, there was no loss of hair, and, in spite of emaciation, restless overactivity was very obvious.

Fraser and Smith (1941) have sought to differentiate between organic pan-hypopituitarism and "functional" anorexia nervosa by estimation of 17-ketosteroids and an insulin-tolerance test. In the organic disorder they found